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PATENT COOPERATION TREATY

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PCT/EP2009/053907

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

HAMMANN, Heinz
Binger Str. 173
55216 Ingelheim Am Rhein
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Eingang CD Patents

19. Okt. 2010

Date of mailing (day/month/year)
14 October 2010 (14.10.2010)

SdT No:

Yes:

Applicant's or agent's file reference
P01-2363/WO

SB gesehen

erledigt

IMPORTANT NOTICE

International application No.
PCT/EP2009/053907

International filing date (day/month/year)
01 April 2009 (01.04.2009)

Priority date (day/month/year)
02 April 2008 (02.04.2008)

Applicant

BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference P01-2363/WO	FOR FURTHER ACTION		See item 4 below
International application No. PCT/EP2009/053907	International filing date (<i>day/month/year</i>) 01 April 2009 (01.04.2009)	Priority date (<i>day/month/year</i>) 02 April 2008 (02.04.2008)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 05 October 2010 (05.10.2010)
	Authorized officer Yolaine Cussac e-mail: pt05.pct@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2009/053907

International filing date (day/month/year)
01.04.2009

Priority date (day/month/year)
02.04.2008

International Patent Classification (IPC) or both national classification and IPC
INV. C07D487/04 A61K31/519

Applicant
BOEHRINGER INGELHEIM INTERNATIONAL GMBH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2009/053907

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2009/053907

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>3-13, 15-18, 28</u>
	No: Claims	<u>1, 2, 14, 19-27</u>
Inventive step (IS)	Yes: Claims	<u>3-13, 15-18, 28</u>
	No: Claims	<u>1, 2, 14, 19-27</u>
Industrial applicability (IA)	Yes: Claims	<u>1-28</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2009/053907

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Claim 27 relates to a subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv)/67.1(iv) PCT.

The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for in a first or further medical treatment.

1) Reference is made to the following documents :

- D1: WO 2004/099210 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BAERFACKER LARS [DE]; E) 18 November 2004 (2004-11-18) cited in the application
- D2: WO 2004/099211 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BAERFACKER LARS [DE]; E) 18 November 2004 (2004-11-18)
- D3: WO 2004/018474 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BOESS FRANK-GERHARD [DE] 4 March 2004 (2004-03-04)
- D4: WO 2004/096811 A (PFIZER PROD INC [US]; BELL ANDREW SIMON [GB]; DENINNO MICHAEL PAUL [US] 11 November 2004 (2004-11-11) cited in the application
- D5: WO 2004/026876 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BOESS FRANK-GERHARD [DE] 1 April 2004 (2004-04-01)

2) Novelty (Art. 33 (1) and (2) PCT) :

D1 and D2 disclose compounds (see claim 1 in both documents wherein R2 is heteroaryl optionally substituted by hydroxy which correspond to a present heterocyclyl group substituted by oxo, see item VII below) having the same activity and falling in the scope of present claim 1, 2, 14, 19-27.

D3 and D5 disclose compounds having the same activity and a closely related structure. They differ however in that no heterocyclic group is present on position 1 of the pyrazolo ring but a pentanyl or a cycloalkyl group.

D4 discloses PDE9 inhibitors overlapping those presently claimed since R3 can be

heterocycloalkyl. None of the example of D4 destroys the novelty of the present application. The present compounds could be considered as a novel selection over those of D4.

3) Inventive Step (Art. 33 (1) and (3) PCT) :

D3 is considered as the closest prior art since it discloses compounds having the same activity and differing from those presently claimed in the definition of the group equivalent to the present H group.

The technical problem underlying the present application is the provision of further compounds active as PDE9A2 inhibitors.

The replacement of the group cycloalkyl by an heterocyclic group is considered as obvious because of the teaching of D4. , which clearly discloses the equivalency of the group cycloalkyl, heterocycloalkyl, aryl and heteroaryl for this family of compounds. No unexpected advantage is disclosed so far for the claimed compounds so that the requirements of the Art. 33(3) PCT are not considered as fulfilled.

Re Item VII

Certain defects in the international application

The group "heterocyclyl" defining Hc should be or comprise a non-aromatic ring according to claim 1 but can also be substituted by an oxo group as indicated in the list defining R². This means that an aromatic ring is still possible e.g. in the case of a dihydroimidazole ring as that mentioned on page 308 second line. A tautomeric form of this structure reveals an imidazole ring (aromatic) substituted by an hydroxy group. The present definition of the compounds of formula I does thus not fulfill the requirements of Art. 6 PCT.